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Multiple Chemical Sensitivity

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Multiple Chemical Sensitivity

This enigmatic syndrome has no generally accepted definition or proved physiological mechanism, yet it is increasingly being recognized in government regulations and the courts

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"Little more than a few months after the occupational medical clinic began at Yale in 1979, the staff was confronted with a problem none of us had ever seen before nor heard about. A middle-aged man was referred because of a delayed recovery from an episode of pneumonia that had resulted from a chemical spill on the job. As his x-ray cleared, he had become not better, but worse. Particularly striking was the history that exposure to chemical odors would markedly exacerbate baseline dyspnea [difficult breathing] and chest pain.

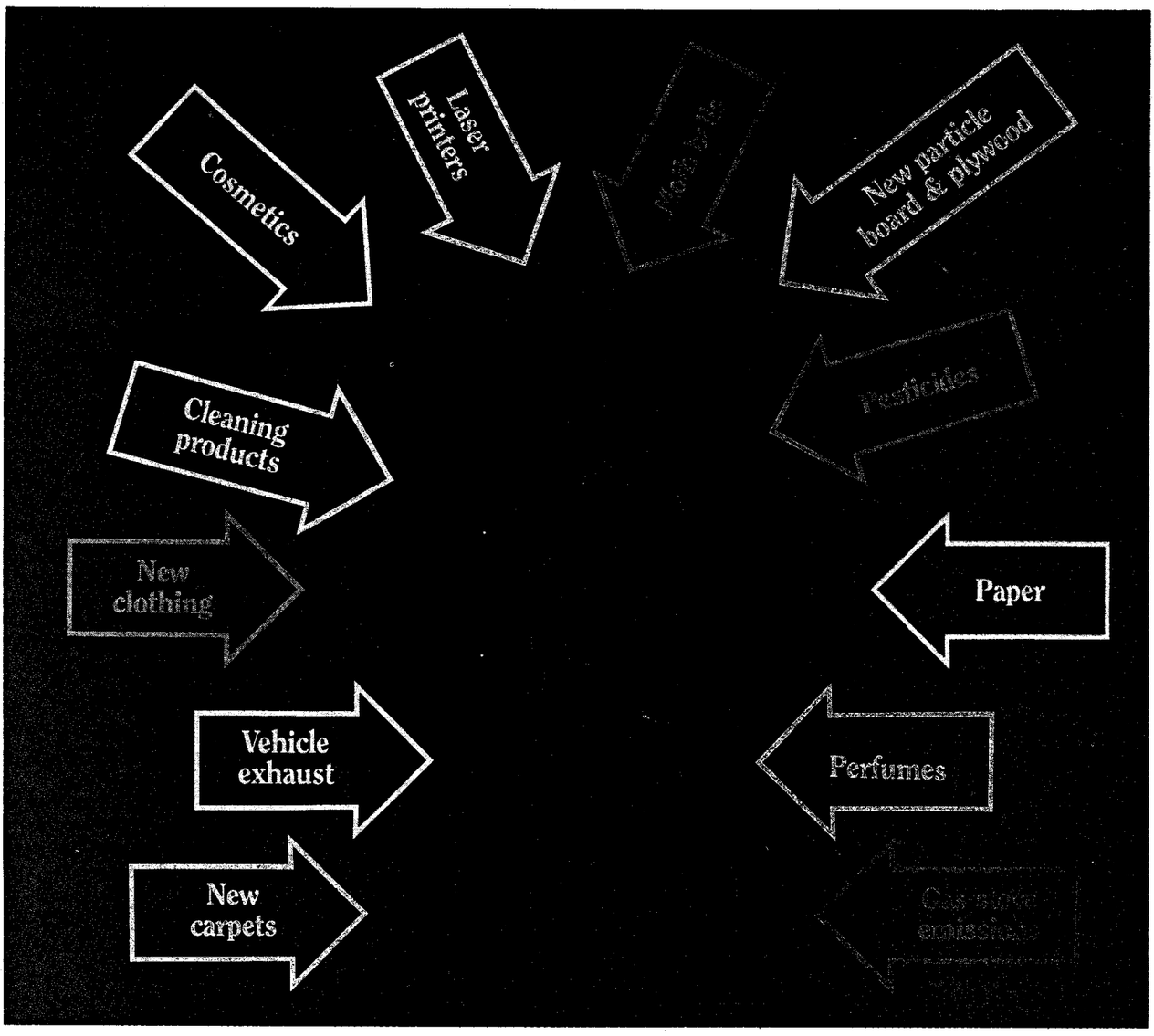
"Upon return to work he 'passed out' on several occasions after a whiff of fume. Disability leave, however, did not resolve the situation. Increasingly, even common household products and environmental contaminants induced debilitating respiratory and constitutional symptoms, reducing his formerly vigorous life to a pitiful existence at home. In response, we exhaustively investigated his list of chemical precipitants in search for some way to tie these toxicologically with his prior pneumonia, but without success. Equally unrevealing were results of extensive clinical tests undertaken to define his 'lesion' pathophysiologically. Therapeutically, it would be generous to say that we accomplished very little. There were other cases too.

"Many of our colleagues practicing occupational medicine around the country began reporting similar cases: They too were stymied by them. Thus we became aware of how widespread the problem is and how incredibly expensive the costs are for medical care and disability in each case."

This passage was written in 1987 by Mark R. Cullen, professor of medicine and epidemiology at Yale University, in the book he edited, titled "Workers with Multiple Chemical Sensitivities," Hanley & Belfus, Philadelphia, Pa. It describes a patient with the most debilitating and striking form of multiple chemical sensitivity (MCS).

Such cases, which have been fairly widely reported in the popular press, comprise only a very small fraction, perhaps 1 to 2%, of people who believe they have this illness. Some of these people are so severely affected they are living in bare porcelain-lined trailers or in tents in rural areas in an attempt to avoid nearly all chemical exposures associated with modern society.

But most people allegedly suffering from MCS have a far less debilitating form of the disease. The majority manage to keep their jobs and maintain a fairly normal home life. They may feel less well at work than they do



at home, suffering from stuffy noses or headaches or rashes. They usually try to avoid the chemical exposures they believe make them feel sick, such as rooms that have been newly carpeted or recently sprayed with pesticides. Sometimes foods they formerly enjoyed now cause serious gastrointestinal upset. They may not be able to tolerate the smell of new clothing in a department store or the odors in the aisles of cleaning products in a supermarket and so they avoid those places. Advocates for MCS patients believe there may be millions of people in the U.S. suffering with frequent headaches or other symptoms who are not aware their problems are caused by their surroundings.

MCS is an enigmatic syndrome to discuss for several reasons. There is a lack of a clear definition of what it is. There is antagonistic and divisive infighting among several medical specialties as they attempt to deal with a class of patients with MCS-like symptoms while defending their professional turf against competing specialties. Plaintiffs and defense lawyers make extreme claims as alleged victims of MCS seek judicial relief in the litigious environment of tort law. And pathos is evinced by reading and hearing the stories of individuals who have experienced severe disruptions in their lives from some causes that are not yet fully comprehensible to modern medical science. Most participants in this drama believe that enough smoke has been observed by reputable scientists and clinicians to support the contention that there is indeed a real fire that society must confront.

Some of the most intense competition and antagonism over this issue is between the allergists and clinical ecologists. (Clinical ecology is the orientation in medicine in which doctors primarily work with patients to uncover the cause-and-effect relationship between their ill health and food or low-level chemical exposures.) Allergists have succeeded in convincing much of the medical profession that the diagnoses and treatment used by clinical ecologists are unproven and ineffective. Some have even called clinical ecologists, physicians who are represented by the Denver-based American Academy of Environmental Medicine, "pseudoscientists." In fact, a large part of the medical profession has become so convinced of the ineffectiveness of clinical ecologists' therapies that physicians who suggest to patients ideas or treatments that are uniquely

Milestones in evolution of multiple chemical sensitivity

Although multiple chemical sensitivity (MCS) syndrome is almost universally called multiple chemical sensitivity in the scientific community today, before 1987 it was known by a variety of names, such as environmental illness, environmental hypersensitivity disorders, chemical hypersensitivity syndrome, ecological illness, and chemical susceptibility problem.

1951 Theron G. Randolph, board-certified allergist, first observes what he called "the chemical susceptibility problem" in one of his patients; this initial observation is later described in the introduction to his book, "An Alternative Approach to Allergies," Harper & Row, New York, 1989.

1975 Environmental control units are opened and operated by Randolph in a Chicago hospital and by William J. Rea, clinical ecologist and member of the science advisory board at the Environmental Protection Agency, in a Dallas hospital to help identify chemicals and foods that provoke symptoms in MCS patients.

1979 U.S. District Court for the District of Hawaii rules MCS disabling and orders Department of Health, Education & Welfare to provide social security disability benefits to Mama Slocum (Slocum vs. Califano).

1984 A California bill to require research on MCS is passed by both houses of state legislature but is opposed by California Medical Association and vetoed by Gov. Deukmajian.

1985 "Report of the Ad Hoc Committee on Environmental Hypersensitivity Disorders" prepared by the Ontario Ministry of Health, Canada, calls for research on MCS and assistance for MCS patients.

1986 American Academy of Allergy & Immunology states in position paper that relationship between MCS symptoms and chemicals or foods is unproven.

1986 Oregon Court of Appeals orders workers' compensation benefits for furniture store employee on basis of MCS (Robinson vs. Saif Corp.).

1987 National Academy of Sciences workshop recommends research on MCS, with assistance from Institute of Medicine and National Institutes of Health, to ensure that fundable proposals are developed; NAS Board on Environmental Sciences & Toxicology takes no action on recommendations.

1987 "Workers with Multiple Chemical Sensitivities, Occupational Medicine: State of the Art Reviews," edited by Mark R. Cullen, professor of medicine and epidemiology at Yale University, Hanley & Belfus, Philadelphia, is published; this is first comprehensive collection of articles on MCS.

1987 California Court of Appeals awards workers' compensation benefits to employee who was found to have developed MCS from long-term exposure to polychlorinated biphenyls (Kyles vs. Workers' Compensation Appeals Board).

1988 EPA employees at Washington, D.C., headquarters become ill when new carpets are installed and other remodeling takes place; some employees eventually develop MCS.

1988 Social Security Administration adds section on MCS to agency's program operations manual for disability determinations.

1989 American College of Physicians in position statement finds relationship between MCS symptoms and chemicals or foods unproven.

associated with clinical ecology risk being disciplined by their local medical boards. Some physicians reportedly are afraid to diagnose people with MCS, or to tell them to avoid certain synthetic chemical exposures, for fear they will be disciplined.

Nevertheless, MCS has been legitimized in a number of federal and state government regulations and proposed bills. In 1990, the Department of Housing & Urban Development recognized MCS "as a disability entitling those with chemical sensitivities to reasonable accommodations" in housing projects receiving federal funding under the Rehabilitation Act. People with MCS are also recognized as disabled under the Fair Housing Amendment Act of 1988. But because of the unique nature of this illness and the almost limitless variety of chemical sensitivities possible, HUD has not yet written a policy that states specifically what reasonable accommodations are required for this disability.

The Social Security Administration also recognizes MCS, which it calls environmental illness, but the agency requires a case-by-case evaluation of this illness, taking into account all symptoms, signs, and lab tests, in order to obtain disability payments. And bills currently being considered in both the Senate and House on indoor air quality identify MCS as one of the health consequences of indoor air pollution.

Those experts who believe that scientific studies have not yet shown MCS to be a true illness are quite alarmed by the government's willingness to legitimize it. "I'm afraid we're going to have a new disease by fiat," says Roy DeHart, president-elect of the American College of Occupational Medicine. "You are going to find that there is a disease whether or not there is a disease. That is what worries me."

As a group, people allegedly suffering from MCS have a large number and range of symptoms they attribute to chemical exposures. The complaints are physical and mental and involve nearly all the systems of the body. The most common symptoms include respiratory problems; headache; fatigue; flulike symptoms; mental confusion and short-term memory loss; gastrointestinal tract difficulties; cardiovascular irregularities; skin disorders; genitourinary problems; muscle and joint pains; irritability and depression; and eye, ear, nose, and throat problems. Some individuals experience only one symptom, but most have more than one.

1989 Rebecca Bascom of University of Maryland School of Medicine prepares report on MCS titled "Chemical Hypersensitivity Syndrome Study" for the Maryland State Department of Environment.

1989 Nicholas A. Ashford, professor of technology and policy at Massachusetts Institute of Technology, and Claudia S. Miller, clinical professor of allergy and immunology at University of Texas, San Antonio, prepare report on MCS titled "Chemical Sensitivity" for the New Jersey State Department of Health; department receives Macedo Award from World Health Organization for sponsoring this work.

1989 Indoor Air Quality Act introduced in Senate addresses MCS.

1989 Ohio Court of Appeals reinstates order of Ohio Civil Rights Commission finding unlawful employment discrimination for dismissal of an employee with MCS (Kent State University vs. Ohio Civil Rights Commission).

1990 (January) In draft position statement, a task force of the American Public Health Association states that government agencies should provide funding for MCS research and that MCS should not be labeled as psychogenic in origin unless environmental cause has been ruled out.

1990 (May) Department of National Health & Welfare in Canada convenes workshop on MCS to develop priorities for research into MCS and to identify health needs of MCS patients; report is issued in January 1991.

1990 (August) U.S. Court of Appeals, reviewing a Minnesota case, upholds MCS as disabling condition under social security disability program (Kouril vs. Bowen).

1990 (August) Pennsylvania Human Relations Commission orders landlord of MCS patient to take measures to accommodate her, including reduction in use of pesticides (Atkinson vs. Lincoln Realty).

1990 (September) Several participants at Congress' Office of Technology Assessment workshop on immunotoxicology threaten to disassociate themselves from final OTA report on immunotoxicity research needs if report addresses MCS.

1990 (September) Indoor air quality bill is passed by Senate, but House bill never reaches floor for vote.

1990 (October) Department of Housing & Urban Development recognizes MCS as disability requiring reasonable accommodations under Fair Housing Act Amendments and Rehabilitation Act of 1973.

1990 (November) MCS patients disrupt San Francisco meeting of American College of Allergy & Immunology at which MCS patients are characterized as mentally ill.

1990 (November) Chemical Manufacturers Association and American Petroleum Institute convene informational conference on MCS called "Perspective on Environmental Illness: An Industry Forum."

1991 (February) Comprehensive review of MCS literature titled "Chemical Exposures: Low Levels and High Stakes," by Nicholas A. Ashford and Claudia S. Miller, Van Nostrand Reinhold, New York, is published.

1991 (March) At request of EPA Division of Indoor Air, NAS organizes workshop of invited experts on MCS; they agree on outlines of research protocol.

1991 (April) American College of Occupational Medicine states in position paper that MCS "syndrome is presently an unproven hypothesis," but that the college supports scientific research into the phenomenon.

The number of chemicals the victims respond to is equally wide, ranging from pesticide residues to vehicle exhaust; household cleaners; perfumes; passive cigarette smoke; formaldehyde in new clothing; fumes from gas stoves; off-gassing of paints, glues, and carpets in new construction; and emissions from carbonless copy paper, laser printers, and newsprint. Most of these triggering agents are irritants or neurotoxins, and many are mixtures of volatile organic compounds. But in some of these complex mixtures it is hard to tell what, if anything, the patient is responding to. The majority of the patients are sensitive to more than one substance, but some react to only one, and the same substance can cause different symptoms in different individuals.

Many patients can identify specific circumstances that initiated their illness. They say their problems began either after an overwhelming chemical exposure, such as a job-related chemical spill, or after a new, chronic, medium-level exposure, such as moving into a new house with significant emissions of volatile organic compounds from the building materials or beginning to work in a new building, often one with poor ventilation. Thereafter, the symptoms seem to wax and wane with low-level chemical exposures, and when exposures are avoided altogether, the symptoms abate or disappear. In an informal survey of some 6800 persons claiming to be chemically sensitive, conducted by a patient group called the National Foundation for the Chemically Hypersensitive, nearly half of the patients say their illness started with a pesticide exposure.

Initially, most patients respond to just one type of chemical exposure, but usually their sensitivities spread to a wider range of agents. In many, sensitivities also expand to include common foods that they used to be able to eat, often a whole class of foods, such as wheat or dairy products. It seems it is the natural constituents of the foods, not the additives or pesticide residues, that provoke the symptoms, though additives and residues often cause problems as well.

Many medical experts find it hard to believe that such a wide range of very low-level chemical exposures could cause such a large variety of symptoms in so many organ systems. Most diseases have a much narrower spectrum of symptoms and signs, so MCS does not fit into the pattern of illnesses physicians are familiar with.

MCS may have existed more than a hundred years ago

There are a number of examples in the literature that indicate that multiple chemical sensitivity (MCS), or something like it, may have existed before the 20th century. In 1880, neurologist George M. Beard described a syndrome called "neurasthenia" or "American nervousness," which seems similar to MCS. Those with this condition had "special idiosyncrasies" in regard to food, medicine, and external irritants. Beard believed diet played an important role and said that these patients improved after fasting for four or five days. He considered neurasthenia mainly a physiological illness, but its root cause, he believed, was modern civilization with its steam power, periodical press, telegraph, science, and mental activity of women.

The famous 19th century French author Marcel Proust seems to have been chemically sensitive. He isolated himself in a cork-lined room most of the time. His biographer recorded a number of instances when Proust showed intolerance to perfume. "My dear friend," Proust would say, "I beg you: shall I be causing you much inconvenience if I ask you to take the handkerchief out of your jacket? You know how I can't bear any perfume."

And on another occasion Proust said, "My dear friend, the last time you were so good as to come and see me—for nobody comes any more to see the wretched invalid that I am—I was obliged to take the chair you sat in and keep it out in the courtyard for three days; it was impregnated with the scent."

In the report on MCS prepared for the state of New Jersey by Nicholas A. Ashford, professor of technology and policy at Massachusetts Institute of Technology, and Claudia S. Miller, clinical professor of allergy and immunology at the University of Texas, San Antonio, the MCS population is divided into four categories: industrial workers; occupants of "tight buildings," including office workers and schoolchildren; people who live in communities where the air and water are contaminated by toxic chemicals; and other individuals exposed to chemicals in consumer products, drugs, and pesticides. Except for industrial workers, females appear to outnumber males in all of these groups.

What are these people suffering from? Are chemical exposures really making them sick? Unfortunately, little has been learned about MCS since Cullen's 1987 book, which, as the first comprehensive compilation of articles about MCS, gave the syndrome its name. Despite the work of various researchers, MCS remains for the most part a poorly understood phenomenon. Some physicians have found treatments they believe help some of their MCS patients, but none claim to be able to help all of them. And they are no closer to finding an objective laboratory test or set of tests to define what, if anything, is physiologically wrong with these people. Many clinical ecologists claim that these patients' immune systems have been damaged. The chemical exposures that allegedly cause MCS, however, do not cause consistent changes in the immune systems of these patients that can be measured with available laboratory tests. And they have not been shown to cause changes in the immune systems of the large majority of the healthy population.

It doesn't help that the disease is known by many different names, including multiple chemical sensitivity, environmental illness, 20th century disease, chemical AIDS, multiple chemical hypersensitivity syndrome, total allergy syndrome, and ecological illness. Although all these terms have been applied to people with MCS, some of the names carry connotations that distinguish them from each other. The sensationalist term "chemical AIDS," for example, which has been used by plaintiffs in a few court trials, implies that chemicals damage the immune system in a catastrophic manner.

Experts from different disciplines disagree with each other about many aspects of the illness—its cause, definition, mechanism, extent, whether it is a new phenomenon, and even its existence as a unique disease or set of diseases distinct from others that are already identified in medical science. Some researchers in this area consider the MCS patient population to be a heterogeneous group who collectively have several different disorders, sometimes even in a single individual.

Broadly speaking, physicians have two theories about what causes MCS: either it is chemicals or it is basically psychological.

To many traditional allergists and psychiatrists, the onset of MCS is due almost entirely to psychological factors. Some consider the syndrome to be a variant of somatoform disorder (the conversion of mental experiences into bodily symptoms) or of posttraumatic stress disorder. Others say that the root problem is an irrational belief on the part of the patients that chemicals are making them sick. For example, John C. Selner, an allergist and respiratory specialist at the University of Colorado Health Sciences Center in Denver, claims that he can cure most of his MCS patients by systemmatically deprograming them to eliminate their "false" beliefs. Similarly, Abba I. Terr, professor of medicine at Stanford University, also thinks chemophobia is the root of these patients' illnesses, although he believes no form of psychotherapy will help many of them.

Other physicians—and these are likely to be clinical ecologists and some traditional physicians who practice occupational medicine—believe that chemical exposures are causing these people to be ill. They think so because of common threads they see in the clinical histories of these patients. Among the most important are that MCS symptoms usually begin after either an overwhelming chemical exposure or a new, chronic, medium-level exposure and that the symptoms diminish when chemical exposures are avoided.

Also, these physicians point to the nearly simultaneous onset of MCS symptoms in groups of patients as evidence that MCS is caused by chemicals. For example, when people begin working in a new building where they are exposed to chemical emissions from new construction materials, sometimes a large number of them independently begin to complain of headaches, stuffy

noses, or fatigue. The symptoms in a small number of these affected workers may then multiply and spread so they are provoked by other chemical exposures encountered at home or elsewhere. The most adversely affected workers seem to become MCS patients whose symptoms began at the same time, presumably from the same exposure. This general sequence of events has occurred in many places across the U.S. during the past decade.

Physicians who believe MCS is caused by chemicals also explain that psychological symptoms in some MCS patients are a natural consequence of suffering from any severely disabling condition. In addition to the financial and social disruptions, having a condition that current medicine has difficulty recognizing and treating further adds to the stresses experienced by these patients. Moreover, physicians argue that chemical exposures may be the direct cause of some of the neuropsychological manifestations exhibited by these patients.

During the past decade, discussions about MCS have almost always turned into emotionally charged battles. For example, when an expert panel, convened last year by Congress' Office of Technology Assessment to prepare a report on immunotoxicity, wrote a chapter on MCS that was part of its original report, most of the chapter was eliminated from the final report because of intense disagreements between some of the panel members. This is but one example of what Cullen has called an "ever widening and hostile debate in which the patient is held hostage and virtually all clinicians are rendered impotent because of widely known intraprofessional disagreements."

Patients report that the controversy over chemical sensitivity within the medical profession makes it difficult for them to find objective information about the issue, and also impedes their ability to obtain workplace accommodations from their employers or financial assistance through government programs. "There is a critical need for constructive dialogue among various provider groups evaluating MCS," states a draft position paper on MCS prepared by a special task force of the American Public Health Association. "This should include scientifically rigorous joint research and educational activities."

The chemical industry and others that use chemicals in their operations and the medical insurance industry have added fuel to this debate. Understandably, they have taken a strong interest in this issue because the trace levels of chemicals that allegedly cause illness are orders of magnitude lower than current regulatory levels. Already thousands of people claiming to be MCS victims have filed lawsuits, seeking either disability benefits or personal injury damages from workplaces or products. In the courtroom, clinical ecologists or specialists in occupational medicine usually testify for the victim, sometimes claiming that chemicals have damaged the patient's immune system. On the other side, allergists or psychiatrists testify for the defendant, often a manufacturer of chemicals or allied products.

Clearly, the economic stakes in this issue are very high. If MCS is eventually verified as a definite medical illness that is clearly caused or exacerbated by exposures to very low levels of chemicals, the chemical industry and other industries whose products seem to cause the illness could be faced with many more thousands of very costly lawsuits. In addition, tens of thousands of workers could claim disability under the workers' compensation and social security systems.

And there would be many other costs—to the individual to change the home environment to avoid chemical exposures, to the employer to lower workplace exposures or move sensitive employees to a less contaminated work area and to add more medical and disability benefit programs, to manufacturers to lower the emissions from certain products, to building owners and managers to upgrade ventilation systems, to the government for expenditures on MCS prevention and treatment, and to medical insurance companies for treatment expenses that currently are often not covered.

On the other hand, establishing a rational verifiable means of diagnosis and treatment for MCS, even if it is caused by chemicals, could save money in some areas. For patients and medical insurance firms, it would avoid the expense of visits to numerous specialists and of repeated diagnostic tests, as is happening now, as patients go from physician to physician in search of a diagnosis and effective treatment. In addition, social services would have established means of evaluating victims of chemical sensitivity. At present, they assess them on a case-by-case basis. And insurance companies would have clear guidelines to use in dealing with worker compensation, disability, and vocational rehabilitation matters.

Other benefits would be that changes could be made in industrial and regulatory systems that might prevent new cases of MCS. And employers and others could perhaps be educated to identify MCS before it becomes disabling and implement less drastic environmental improvements than would be required with the full-blown illness.

Disagreements in definition

There is no definition of MCS that is accepted by all experts in the field. Even getting enough consensus so the disease can be studied is difficult. A workshop convened in March by the National Academy of Sciences to develop a research program on the syndrome came up with this definition of MCS patients for case selec-

Ten volatile organics dominate emissions from modern building materials

n-Decane	1,2,4-Trimethylbenzene
Ethylbenzene	1,3,5-Trimethylbenzene
n-Nonane	*n*-Undecane
n-Propylbenzene	*m*-Xylene
Toluene	*o*-Xylene

Source: *Environmental International* [8, 122 (1982)]

One person's encounter with multiple chemical sensitivity

In the following condensation of an article in Perspectives in Biology & Medicine *[[34:3, 355 (1991)] copyright by the University of Chicago. All rights reserved], Philip Klubes, professor of pharmacology at George Washington University Medical Center, describes his own encounter with the most acute form of multiple chemical sensitivity (MCS). His experience with the illness was typical in many ways, but atypical in that he recovered almost completely.*

"As 1987 drew to a close, my life seemed routine as I attempted to meet the various professional responsibilities of a 52-year-old professor of pharmacology. I was unaware of the existence of the syndrome of MCS. Sometime around Christmas 1987, I developed itching and irritation on my face and neck that increased in severity; eventually my eyes and eyelids also become affected. On March 1, 1988, I was seen by a dermatologist at our medical center and diagnosed as having a contact dermatitis of unknown etiology.

"I was particularly concerned that the symptoms occurred primarily when I was at my desk and usually subsided once I was out of my office. Surprisingly, my laboratory, adjacent to my office and full of many chemicals and solvents (that is, potential sensitizers), was a haven compared to my office. There was some persistence of the symptoms at home, but my office seemed to be the prime offender. My small, windowless office overflowed with a floor-to-ceiling accumulation of books, papers, journals, reprints, catalogs, and so on.

"By the second week in March, while working in my office, I noticed that, in addition to my facial irritation, my eyes felt full and watery. Apparently, my eyes had now also become sensitive to the same irritant(s). Soon I began to notice that the sensation of watery eyes increased when I tried to read either new journals or some books. On April 11, I underwent the Standard North American Group (22-compound) Patch-Test Screen in an attempt to determine the basis for my ongoing contact dermatitis. The only positive response was a mild reaction to formaldehyde (+1 on a scale of 1 to 4). My dermatologist and I were aware that formaldehyde is used in paper processing, and high concentrations persist in paper and paper products. I was pleased to have a possible explanation for the problem I was experiencing and relieved that my formaldehyde response was quite mild.

"Aware now of the likely cause of my contact dermatis, over the next few days, I emptied my office and moved my books, journals, papers, and file cabinets into my lab. As a precaution at home, my wife and I began to clear out my den, and move the books, journals, and files, as well as the other books in the house, into the back basement.

"On Sunday, April 17, a new problem developed; while reading the *New York Times* I experienced the now familiar sensation of watery eyes and, in addition, became aware that the paper had a noticeable odor. On April 20, all my anxieties peaked during a faculty meeting. While reading a photocopy of a research grant application, I detected a distinctly unpleasant odor, my eyes began to water, and I began to feel faint. I ended up in the office of my internist; however, my physical examination revealed nothing abnormal. As I left his office, I realized that, for the first time in my life, I had suffered an anxiety attack, apparently because I had been overwhelmed by the fear that if I had problems reading the application, perhaps I would not be able to work at all.

"Over the next few weeks my condition continued to worsen. For the first time, reading a journal, book, reprint, or even a memo not only caused watery eyes. In addition, I felt burning, stinging pinpoint pain on my face and mucous membranes of my inner eyelids. Isolated, seemingly unrelated incidents made me realize that other things, for example, assembling cardboard file folders to store reprints or looking at newly developed photos, could also cause the same pain.

"April 29 was marked by epigastric distress, presumably signaling reactivation of a quiescent duodenal ulcer, a legacy of my climb to tenure. On May 2, I was seen by an allergist. I described to him how my sensitivity, which had begun with journals, books, and papers, was now spreading so that other things triggered off the same painful symptoms, and in addition, I smelled unusual odors. He told me that I had a syndrome known as MCS, and he estimated it might take six months or more to subside. I was ecstatic because now I had a diagnosis.

"To minimize contact with and exposure to paper, I was to wear my lab coat, disposable cotton gloves, and a surgical face mask. In addition, I could air out my new journals in a laboratory fume hood before trying to read them. Books and even newpapers could be "baked" in a laboratory drying oven at 150 to 200 °C for about 10 minutes.

"The next day at work I donned a surgical face mask, disposable gloves, and my lab coat. As added protection I wore a Plexiglas safety face shield. I soon found that this outfit was not only ineffective but also caused its own problems. Each morning, after a few hours at my desk, the surgical mask itself developed a strong odor, and my face and eyes became even more irritated. In addition, baking journals or papers removed one set of odors only to create new odors reminiscent of charred paper. Walking around the department, peering out from behind my surgical mask and face shield, gave me the first intimation of the sense of vulnerability to the environment and social isolation often characteristic of patients with MCS.

"Within a few days, and despite this 'protective' outfit, my sensitivity to the odors from journals, books, and particularly newspapers, dramatically increased. Newspapers now had an intense, objectionable odor best described as a stench, and I could not remain in the

ıion for research purposes: Patients must have symptoms or signs related to chemical exposures at levels tolerated by the population at large. (Reactions to such well-recognized allergens as molds, dusts, and pollen are not included.) The symptoms must wax and wane with exposures and may be expressed in one or more organ systems. A chemical exposure associated with the onset of the condition doesn't have to be identified, and preexistent or concurrent conditions—such as asthma, arthritis, or depression—should not exclude patients.

But Cullen, for one, would define the condition more restrictively. He says the symptoms must be expressed in more than one organ system—that is, there must be more than one symptom—and the disorder must begin with some documentable environmental exposure, in-

same room with one. My sensitivity to books now had increased to the point that just walking past a shelf full of books triggered off the familiar sensation of stinging and burning pain on my face and eyelids. One morning, while at work and dressed in my now standard outfit, I began to open one of my file cabinets. Suddenly, I was repulsed by a powerful stench together with intense burning, stinging pain on my face and inner eyelids; it was as if there were an open tear gas cannister in the drawer. I borrowed an industrial-grade, full-face mask respirator from the Medical Center Safety Office. This respirator, equipped with two adsorbent cartridges, was capable of excluding formaldehyde and various other volatile organic compounds.

"By the second week in May, all the books in our house had been moved into the back basement. The process of sorting the books increased, for me alone, the stench of books throughout the house. This odor, plus the pain to my face and eyes, became so severe that when I went into the basement I had to wear the respirator. Within a few days all the books we wished to save were put into storage and the rest were donated to a charity.

"Because of my increasing sensitivity, work was not only frustrating—it seemed impossible to continue on a full-time basis. I discussed with my allergist how my sensitivity to paper continued to increase despite the precautions I was taking. He assured me that my course was not unusual and suggested that I take two weeks off from work in the hope that this would 'turn things around.'

"Over the weekend of May 14 to 15, I noticed some improvement. On May 17, I found to my surprise that the daily newspaper, which previously had created a powerful stench, now produced only an objectionable odor. May 17 was a turning point, the first in what up until now had been a long downhill slide.

"During the weekend of May 21, I became aware that I was now sensitive to various scented products (none of which I used myself) such as men's after-shave lotion, women's cosmetics, moisturizing lotions, and fragrant soaps. During the remainder of May and throughout June, my condition steadily improved; however, my list of new (and surprising) sensitivities continued to increase. Removing the books from our house turned out to be only the first step in a "forced" redecoration which over the next few months also included other items, for example, carpets, drapes, and some foam-filled furniture. For the first time, upper respiratory tract irritation manifested by coughing, chest pain, and some dyspnea occasionally occurred when I was exposed to some substance, for example, cosmetics, to which I was sensitive.

"After my sudden improvement of May 17, I had gone back to work, although on a curtailed schedule. By taking appropriate precautions, which included the use of goggles, plastic face shield, gloves, and a desk fan, I was able to work, although at a disappointingly slow pace. Nevertheless, the multiplicity of things that could provoke symptoms continued to frighten and amaze me. It was as if everywhere I went my environment turned on me. Invariably these new sensitivities took me by surprise. A sampling of the list, which seemed endless, included carbonless copy paper, new permanent-press pants, driving in an enclosed car with the air conditioner or heater on, riding the subway, pumping self-service gasoline, going into an enclosed shopping mall, walking past the clothing section of a department store, cooking on the gas stove at home, using felt-tipped pens, and (everywhere, it seemed) carpets both old and especially new. I found, as a patient with MCS, many routine tasks of social interactions now became an environmental encounter, and there came a feeling of social isolation.

"The biggest surprise, however, occurred one morning at home while I was revising a lecture at my computer. After about an hour, my eyes and face began to sting, and I developed some upper respiratory tract irritation. It took several days of experimentation to conclude that the source of my problem, whatever it was, was coming out of the exhaust vent at the back of the computer.

"On July 1, by referral, I was seen by an allergist who had a particular interest in MCS. After a lengthy interview, she informed me that, although I had experienced a marked improvement, it was probable that, like other MCS patients, I would always have some predisposition to the syndrome. My physical examination was unremarkable. She cautioned me about the need, in the coming months, to be very careful and to avoid any unnecessary exposure to irritants.

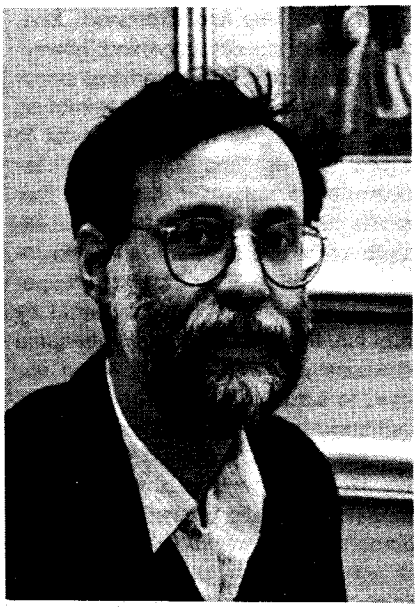
"I continued to improve during July and returned to work, on a regular daily basis, on August 1. A few days after returning to work, I noticed that the ventilation in my office seemed inadequate. I subsequently learned that some time during the past year, while undergoing routine service, the office exhaust vent had been capped and never reopened. The vent was soon restored to working order. The fact that the exhaust vent had been cut off for some time, probably prior to the onset of my initial symptoms, provided a probable (or at least partial) explanation as to why my original difficulty centered around my office. Presumably, the poor ventilation in my windowless office had allowed for the accumulation of volatile organic compounds which offgassed from my stacks of journals, books, and papers.

"The semester began at the end of August and I was back in the full cycle of the academic year. During the remainder of 1988, I continued to make slow, steady progress toward approaching a kind of normality, albeit with some compromises, at work and at home. Eventually reading no longer required the use of a plastic mask, book shield, or desk fan. Later that semester, I was back in the lab, carefully using various organic solvents, while setting up a high-pressure liquid chromatography assay to measure plasma drug levels in cancer patients undergoing chemotherapy. By spring 1989, during office visits to both my allergists I demonstrated my ability to read several new journals with only some difficulty."

sult, or illness. In this way, patients with long-term health problems who later begin to attribute them to chemical exposures are excluded. Cullen also says that the chemical exposures to which the patients respond must be demonstrable—in other words, people other than the patient must be able to smell the offending agent even though they are not reacting to it. Such a condition would exclude frankly delusional patients or those that believe chemicals "must be present" whenever they feel ill. Cullen would exclude from his definition patients who have a disease already recognized by the medical community, such as asthma. Ashford and Miller, as well as the NAS workshop participants, view Cullen's definition as overly restrictive. They reason that the disease may start with only one symptom, which could very well be asthma or rhinitis, and that

the disease may be easier to study in the early stages when only one symptom has developed.

However, Cullen thinks it's important to define cases for study very restrictively, or researchers may end up studying a diverse group of patients who have several different illnesses. DeHart of the American College of Occupational Medicine also objects to the research definition agreed to at the workshop. He thinks that medical scientists cannot begin to study MCS until a narrow definition is established and accepted. The definition must be "specific enough that you can establish a cadre of patients that can be considered those that are suffering from this manifestation," he says. "The more restrictive you are, the better chance you have of finding whatever the common denominator is among these patients."



Cullen (left): study cases need restrictive definition. Davis: 500 new inquiries each month

Exacerbating the disagreement over the definition of MCS is that different interest groups have their own reasons for establishing a definition. Patient groups fear that if a definition is too narrow, so that it leaves out categories of patients who really have MCS, these patients will be excluded under future laws and regulations that may provide benefits for MCS victims.

"No single case definition, even if agreed upon in one context, will suffice for use in other contexts," MIT's Ashford says, so a definition that's useful in designing a study may not be the appropriate one for setting regulatory standards or awarding compensation to workers with the disease. However, in the U.S. the case definition established for research has in many instances been used later for other purposes, such as awarding disability benefits.

Prevalence may be increasing

The lack of a clear definition or diagnostic test for MCS makes it very difficult to estimate its prevalence. However, there is much indirect evidence that the number of people diagnosed with MCS is increasing. A large body of anecdotal material describes patients who fit the general criteria for this illness. Also, the number of physicians treating these patients has gone up dramatically in the past decade. During the same time period, the volume of sick-building complaints, some of which are registered by people with MCS, has also risen rapidly. Earon S. Davis, environmental health adviser to the National Center for Environmental Health Strategies, a national advocacy center for chemically sensitive patients, says about 500 new people contact the center each month to inquire about how to deal with MCS problems. Ten years ago only about 100 people were contacting national groups each month. Political and scientific activity in the MCS area also has intensified greatly.

On the other hand, more patients seeing more physicians about problems related to chemical exposures may be a sociological rather than a clinical phenomenon. Cullen suggests that chemicals may be playing a surrogate role for anxieties and frustrations in society. What may have changed is people's perceptions of chemicals, which leads them to try to find a chemical explanation for their illnesses. However, there is a subset of individuals who, after experiencing a chemical exposure that is noxious, do go on to react to chemicals at low doses, he says. He doesn't know whether this group is growing.

Carroll M. Brodsky, psychiatrist at the University of California School of Medicine, San Francisco, says, "There have always been people who have had unpleasant physical and emotional symptoms for which they sought explanations." Many of these people are now seeking treatment from clinical ecologists because they offer them an explanation, he says, often that low doses of chemicals are causing their problems.

If the prevalence of MCS is increasing, is it because people are being exposed more to chemicals or that they are being exposed to some particular new substances that are especially noxious? Such questions, too, are controversial and exposures are difficult to measure. Americans, who, on average, stay indoors about 90% of the time, do spend more time indoors than they did in previous generations, and usually the levels of volatile organics are much higher in indoor air than they are outside. Also, there is increased use indoors of materials and equipment, such as carpets, wall coverings, copiers, and particle board, that emit volatile organic chemicals.

And since the Arab oil embargo of 1973, efforts to improve the energy efficiency of buildings have made buildings tighter, allowing more indoor air contaminants to accumulate inside homes and office buildings. In commercial buildings, for example, ventilation standards, which once required 10 cubic feet per minute of fresh make-up air per occupant, were reduced in the

mid-1970s to 5 cfm per person. In 1989 a new voluntary standard was set at 15 cfm per person, but the ventilation rates in most buildings constructed under the 5 cfm standard have not been increased. New homes, too, have about half as much fresh air infiltration as homes constructed before the mid-1970s.

Exposures to some specific contaminants have increased and others decreased over the past few decades. Exposures to terpenes used in deodorizers, waxes, and polishes have increased. Pesticide use on lawns and as insect sprays in buildings has risen. And the sheer number of different chemicals to which people are exposed has risen greatly. EPA receives about 10 new premanufacturing notices each working day, which results in more than 1000 new chemicals a year finding their way into commerce.

Some exposures, though, have dropped dramatically. Carbon tetrachloride is no longer allowed in household products and the benzene content of gasoline has been cut. For blue-collar workers, overall chemical exposure has probably diminished, thanks to standards set by the Occupational Safety & Health Administration in the late 1970s for some well-known air contaminants, such as coke oven emissions. But new products are continually being introduced, and workers involved in their manufacture are exposed to mixtures of new low-level contaminants about which very little is known.

Speculative mechanisms

Several mechanisms—all highly speculative—have been proposed to explain MCS. Any useful model needs to explain how symptoms can occur in almost any system in the body, and how sensitization can be triggered by a wide range of chemical agents and spread to include other substances with no obvious chemical structural relationship. It must explain as well triggering by lower levels of chemicals than those that initiated the illness, and subsequent food intolerances.

Recently, a mechanism involving the limbic system of the brain and the interconnected olfactory system has received considerable attention. It was discussed extensively at the workshop on MCS arranged by NAS in March. The mechanism was first proposed and developed by Iris R. Bell, a psychiatrist at the University of Arizona, and has also been developed by Miller in the comprehensive review of the literature, "Chemical Exposures: Low Levels and High Stakes," which she coauthored with Ashford.

The olfactory system is the normal pathway by which airborne chemicals intereact with the brain; and the limbic system, which is located very close to the olfactory bulb, is the focal point in the brain where the immune, nervous, and endocrine systems interact.

Bell and Miller speculate that the hypothalamus, which communicates directly with the limbic system and has known links to the olfactory system, could be directly involved in the MCS syndrome. The hypothalamus acts as an analytical laboratory, computer controller, and hormone controller for the entire body. It governs body temperature; reproductive physiology and behavior; feeding, drinking, and metabolism; and aggressive behavior. It also influences some functions of the immune system, sends electrical signals to the nervous system, and produces its own hormones.

Because the hypothalamus is involved in so many physiological functions, disrupting it could have consequences in many different parts of the body. If chemicals reaching the olfactory nerve endings in the nose could be transported into or relay electrical signals to the hypothalamus or to other interconnected parts of the limbic system, "resultant dysfunctions in numerous behavioral, autonomic, and endocrine subsystems under limbic regulation might then lead to multiple symptoms through a range of end-organ mechanisms," Bell says.

Chemically sensitive patients may have olfactory-limbic-temporal pathways that are readily "kindled," Bell says. In regions of the brain where kindling is present, a small signal that ordinarily would not cause nerve cells to fire, readily triggers firing. Consequently, common low-level contaminants, such as tobacco smoke, could conceivably trigger symptoms in individuals whose limbic areas have been kindled by a prior large exposure of a contaminant, Bell explains.

"Even unperceived low concentrations of airborne chemicals can induce changes in brain electrical activity and resultant behaviors and physiology in both animal and human subjects," says Bell. For example, in rabbits initially exposed to a high concentration of pollutants, subsequent low concentrations combined with a rhythmic flashing light "triggered abnormal paroxysmal activity [abnormal firing] in the olfactory bulb and

In their report for the state of New Jersey, Miller (left) and Ashford divide MCS population into four categories

Alleged sensitivity to carpets at EPA led to a dialogue with the carpet industry

An early incident that brought multiple chemical sensitivity (MCS) to national attention began in late 1987 and early 1988 when the Environmental Protection Agency installed 27,000 square yards of new styrene-butadiene-latex-backed carpet in many of the offices at its national headquarters in Washington, D.C. The ventilation rates in most of these offices were very low. Within a few days, some employees began to complain of respiratory problems, burning eyes, rashes, dizziness, and nausea.

After a few months, more than 122 employees had complained of adverse health effects that they blamed on poor air quality and carpet emissions. In response, the suspect carpet was removed and replaced by high-density polyurethane foam-backed carpet. But 45 or 50 of the employees say they have been sensitized so strongly by carpet fumes or by emissions from other new building materials that were being installed at the same time as the carpet that they continue to feel sick when they go back into the buildings where the carpet was installed. Today these people work at home or in offices in specially constructed facilities where the floors are bare and the windows open.

In 1988, J. William Hirzy, then president of the National Federation of Federal Employees, Local 2050, the union of professional employees at EPA, testified before a Congressional committee about the employees who allegedly had become chemically sensitized. And in 1989, several EPA employees who believed they suffered acute health effects from the suspect carpet also testified before Congressional committees during hearings on indoor air bills. These hearings led to extensive media coverage of health effects people say they suffer from carpets.

As a result, people from all over the country began contacting the EPA union about health problems they believed they were having from the installation of new carpet. In early 1990, the union leadership and its members became convinced that carpet could cause serious health problems and petitioned EPA on behalf of agency employees to take emergency regulatory action to address the threats from new carpet.

A group of agency experts reviewing the petition found there was no evidence that carpet poses enough risk to warrant emergency action. As a result, the petition was denied. Instead EPA promised to initiate discussions between members of the carpet industry and the public, called a "carpet dialogue." At monthly meetings, officials of EPA's indoor air office

[a part of the limbic system called the] corticomedial amygdala."

No human studies have yet been done to test the validity of the proposed limbic mechanism because the theory is quite new and there are no laboratory markers that indicate what is happening in the limbic system. Eventual research to determine if the limbic system does indeed play a role in MCS will probably require elaborate tests of brain function.

Another mechanism proposes that MCS occurs when the immune system is damaged by chemical exposure. According to this theory, which has been advanced by a large number of clinical ecologists and other investigators, initial high-level exposure or chronic low-level exposure causes the immune system to overreact to subsequent exposures or to lose some of its ability to protect the body against harmful substances. The immune system, which performs the well-known function of defending the body against harmful microorganisms, also carries out precise regulatory interactions between itself and the endocrine and nervous systems. Therefore, a dysfunction in the immune system could possibly lead to a multitude of symptoms, as well as to an intolerance to subsequent exposures.

Common allergens, such as pollen and mold, produce elevated levels of the immunoglobulin class known as IgE, a component of the immune system. In MCS patients, the IgE level is usually normal or lower than normal. But the levels of some other components of the immune system can be abnormal. Alan S. Levin, professor of immunology at the University of California, San Francisco, found that T cell and B cell counts and the ratio of helper T (T4) to suppressor T (T8) lymphocytes are altered in the immune systems of MCS patients. Similarly, William J. Rea, a clinical ecologist in Dallas, Tex., found abnormal levels of complement, T lymphocytes, eosinophils, and the immunoglobin known as IgG in a study of the immune systems of a chemically sensitive patient group.

But research findings are not consistent on this point. Stanford University's Terr found normal levels of immunoglobulins, complement components, and lymphocyte subsets in a review of the medical records of 50 patients diagnosed with MCS. Levin disputes these findings, saying that the levels of these components fall outside the normal range in 20 to 30% of the patients Terr reviewed, whereas in the general population only 2.5% would be expected to fall outside the normal range. He concludes that many of Terr's patients had abnormalities in their immune systems.

Some researchers, Cullen, for example, doubt that irregularities in the immune system could cause MCS because this system is very specific in the way it reacts to chemicals and so could not respond to a wide variety of compounds. But Robert G. Burrell of the department of microbiology and immunology at West Virginia University argues that immunologists have come to realize that "the very same immune system that recognizes specific antigens can also be stimulated nonspecifically to carry out its effects independently of antigens."

It is sometimes this immune system model of MCS that is used in lawsuits filed by MCS patients seeking compensation for the costs of their illnesses. In such cases, lawyers for patients have tried to convince the jury that their clients' immune systems have been damaged by chemicals and that this is responsible for their symptoms.

and representatives of the Carpet & Rug Institute, the EPA union, carpet manufacturers, public interest groups, the Adhesives & Sealants Council, the Consumer Product Safety Commission (CPSC), and the National Institute of Occupational Safety & Health discuss ways to quantify and lower total volatile organic emissions from new carpets.

The dialogue has made progress in several areas. The Carpet & Rug Institute has agreed to conduct a major study to define carpet-emission decay characteristics and to study and compare the various types of carpet. Also, the introduction by many manufacturers of an entirely new class of low-emitting adhesives for carpets has been accelerated.

Meanwhile, New York Attorney General Robert Abrams received hundreds of complaints about alleged health effects from new carpeting and the glues that are used to install them. Consumers complained of "flulike symptoms, rashes, worsened respiratory conditions, asthma, and permanent multiple chemical sensitivities, following exposure to new carpet materials," Abrams says. He was particularly alarmed by the deaths of two men that occurred when they were gluing down carpet in an enclosed area on a boat. In April of this year, Abrams petitioned the CPSC to require warning labels on new carpets and installation materials. He also asked for a comprehensive education program that would include posters in stores and free pamphlets "to alert consumers to the potential health hazards of new carpeting."

Robert B. Axelrad, director of the indoor air division at EPA, then wrote to Abrams, saying Abrams did not have sufficient information to warrant health hazard warnings for carpets. He said there was no need to petition the CPSC because voluntary industry changes resulting from the carpet dialogue might lead to carpets with lower emissions. The EPA union disagreed. It also wrote Abrams, saying it prefers an immediate regulatory approach, even though it recognizes that some progress has been made through the carpet dialogue.

The carpet issue represents a contrast between the philosophies of two groups at EPA. One, the indoor air division, has taken a conservative nonregulatory approach. It is working with the carpet and rug industry to persuade it to reduce carpet and glue emissions voluntarily. The EPA union has taken a regulatory protective approach. Ironically, however, the indoor air division did not initiate the carpet dialogue until the EPA union petitioned the agency for immediate regulatory action on carpets.

Several researchers find the evidence weak that MCS is caused solely by disruption of the immune system and suggest instead that the immune system acts together with the nervous system to produce the syndrome. William J. Meggs of the department of medicine at East Carolina State University, for example, proposes that volatile organic chemicals irritate fibers in the airway, leading to inflammation. As the airway becomes inflamed, lymphocytes attack tissue proteins that are bound to the chemicals. This process "leads to sensitized lymphocytes specific for the chemicals that were present in the airway. Subsequent exposure to these chemicals can lead to the production of cytokines [chemical messengers] which ... may affect the central nervous system," Meggs says. Because the nervous system controls blood flow in vessels throughout the body by controlling smooth muscle function, its disruption could cause diverse and seemingly unrelated symptoms in many organ systems. This theory is so new that no research has been done yet to test its validity, but Meggs feels it would be very amenable to study in animal models.

Psychological mechanisms

In contrast, a number of allergists and psychiatrists speculate that psychological mechanisms are largely or completely responsible for the symptoms of MCS patients. DeHart thinks behavioral conditioning to odors very similar to Pavlov's classical conditioning experiments with dogs is responsible for illness in some of his patients. He says he can help these patients by deconditioning them. After first establishing that he can't find any organic basis for their symptoms, he asks his patients to "be specifically sensitive to the idea that suggestion plays an important role in their symptoms"—in other words, to be open to the notion that the mere perception of an odor may cause the onset of their symptoms.

John E. Salvaggio, professor of medicine at Tulane University School of Medicine, says MCS should be classified among the somatoform disorders. (He defines such disorders as conditions in which physical symptoms suggest organic disorders for which there are no demonstrable organic findings or physiologic mechanisms and in which psychological factors are presumed to be part of the cause.) "Personality profiles of [MCS patients] are often markedly abnormal, indicating deeply rooted psychoneurotic problems with features of depression, hysteria, somatization of symptoms, and little insight into their symptoms," Salvaggio says. He believes that little can be done to help these patients.

Denver allergist Selner, who says he can cure 50 to 75% of his MCS patients with systematic deprograming, claims to have found a "disturbing incidence of life-threatening physical abuse and sexual abuse in early childhood among these patients." The success of deprograming depends on the extent to which the "ecologic" belief (the belief that chemicals are the cause of their symptoms) is needed by the patient to avoid confrontation with painful life experiences, he says. He used low-frequency electroencephalographic patterning to compare 36 MCS patients with a group of 71 people who have well-characterized psychological impairment and found many similarities between the two groups. However, he has not published any data or details concerning his MCS patients in peer-reviewed literature.

Donald W. Black, a psychiatrist at the University of Iowa College of Medicine, compared 26 MCS patients

There are no laboratory markers for MCS

Part and parcel of the difficulty in defining multiple chemical sensitivity (MCS) is that there is no laboratory test or set of tests that can be used to diagnose it. According to the report on immunotoxic substances prepared by Congress' Office of Technology Assessment, " 'true allergies' occur when a human comes in contact with a substance that triggers a predictable response that involves certain components of the immune system." The foreign substance triggers a response in the immune system that can be measured with laboratory tests. The most common allergy tests measure immunoglobulin (Ig) levels in serum, usually the Ig class known as IgE. In the case of IgE, the radioallergosorbent test (RAST) is used to identify antigen-specific antibody.

Chemical exposures that allegedly cause MCS, however, do not cause consistent changes in the immune system that can be measured with available laboratory tests. Some researchers claim that immune system damage in these patients is the cause of their illness, that, for example, the patients' ratios of helper T (T4) to suppressor T (T8) lymphocytes are abnormally low. However, when all studies of T4 to T8 ratios in these MCS patients are examined, many cases are at the lower end of the normal range, but some are elevated, and some are not affected at all.

In court cases involving MCS patients, however, lawyers for the patients sometimes claim that the plaintiffs' T4 to T8 ratios have been depressed, thereby causing their symptoms. It is difficult to prove immune system damage because normal ranges for many immune parameters have not been well established.

A mechanism for MCS involving the limbic system of the brain and interconnected olfactory system has received a great deal of attention lately. Researchers speculate that if chemicals reaching the olfactory nerve endings in the nose could be transported into or relay electrical signals to the limbic system and cause dysfunctions in numerous subsystems under limbic regulation, this might lead to multiple symptoms in many organs.

However, there are no lab markers that indicate what is happening in the limbic system. If the mechanism for MCS involves the limbic system, there may not be a convenient lab marker for the illness, says Claudia S. Miller, allergist and immunologist at the University of Texas, San Antonio. So it may never be easy to diagnose MCS on the basis of lab tests.

with 46 age- and sex-matched community controls and found 17 (65%) of the MCS patients met criteria for a current or past mood, anxiety, or somatoform disorder compared with 13 (28%) of the control group. He concludes that psychiatric disorders could explain some or all of the symptoms of these patients.

However, his work has been strongly criticized by other researchers who argue that a healthy group of people is not an appropriate control for chemically sensitive patients. MCS is a chronic illness, which in itself may lead to psychological problems, such as anxiety and depression. Thus, a proper control group for MCS patients would be a cohort of chronically ill people, like those suffering from severe chronic back pain, they say.

And even if MCS patients have more psychological problems than average, perhaps that means that major psychological trauma causes physiological alterations in individuals so that they are likely to develop sensitivities to chemicals, Ashford says. The mere presence of a greater than average number of psychological problems in these MCS patients does not establish that MCS is a psychological illness, he argues.

Still other experts, including Bell, propose that physiological and psychological factors—and possibly social factors as well—may interact to cause MCS. "A dichotomous view of MCS is overly simplistic," Bell says.

The theory that MCS is caused solely by psychological factors infuriates many patients. It seems demeaning and unfair to them to be diagnosed as a mental patient when they believe toxic chemical exposures caused their illness. The psychiatric diagnosis serves to diminish their ability to gain cooperation from others and takes away many of the legal rights they seek to assert. Friends and family are less likely to help them reduce chemical exposures at home, and employers are less likely to make special accommodations for them—such as providing them with a work area with fewer air contaminants.

Economically, the psychiatric diagnosis can be disasterous. It eliminates the chance for compensation through personal injury litigation and makes workers' compensation unavailable in many states. Psychiatric diagnoses also make it difficult for patients to secure health and disability insurance benefits, Social Security disability, and other "safety net" benefits. This is because of the limited coverages for psychiatric disorders under most insurance plans and the frequent assumption that the patient is malingering because the nature of the psychiatric diagnosis is also vague—for example, somatization disorder or affective disorder—and not always disabling.

Last year at the November meeting of the American College of Allergy & Immunology, Denver allergist Selner led a workshop with psychologists and psychiatrists on the theory that psychogenic factors are the primary cause of MCS. This outraged the MCS patients who, with help from the AIDS activist group ACT UP, the AIDS Coalition to Unleash Power, were picketing outside the building where the workshop was being held. Several patients arrived at the workshop and began accusing the physicians of dismissing them as crazy. They so disrupted the meeting that it was called to a halt for several minutes.

Ashford thinks patients have a legitimate interest in trying to convince physicians to take their problems seriously and to consider the possibility that MCS symptoms are indeed triggered by chemicals. Patients should

have some role in ensuring that research trials are well conducted and designed to test more than just psychological mechanisms, he says. Panels set up by the National Institutes of Health to establish research priorities usually include patient representatives.

But other medical scientists—Cullen, for example—believe that in attempting to influence research, patients are interfering with the proper conduct of science. "People with the disease have become very active in the community that is studying the disease," he says. "Patients have built up a huge internal network so they communicate very rapidly with each other. They are suspicious about who is doing what kind of research, posing what kinds of questions. And it's become very hard to do studies."

Patient advocates insist, however, that the difficulties in doing studies are caused not by those with the illness but by pressures mounted by vested interests opposed to research that may find a physiological basis for MCS.

Diagnosis and treatments

With so much controversy within the medical community about what MCS is, it's not surprising that patients receive widely different treatments depending on the kind of physician they go to. Most clinicians take complete medical histories of chemically sensitive patients. And all make an effort to identify chemicals, biological inhalants, or psychological factors that could cause the patients' conditions. However, the degree of attention to environmental exposures, food-related symptoms, and psychological factors varies tremendously based on the physicians' attitudes toward the illness.

The therapies offered by allergists and clinical ecologists differ markedly. Allergists recommend avoidance of suspect chemicals or foods if they believe a true sensitivity exists and if the avoidance is practical. They also use drugs, such as antihistamines and topical and systemic steroids, to treat the condition. Ecologists place much more emphasis on avoidance of chemicals and foods that seem to cause problems, sometimes recommending the construction of "safe" houses or "safe" rooms—those made of building materials that have very low chemical emissions—for the patient. They also use rotary/elimination diets to control reactions to chemicals and foods. To help patients eliminate toxins stored in body fat, some recommend special saunas and vitamin therapy. They prescribe prescription drugs much less often than allergists do.

If allergists decide they can't help patients, they often refer them to psychiatrists. Clinical ecologists may also refer patients to psychiatrists if patient histories and testing do not demonstrate consistent sensitivities. However, they are much more likely to make the MCS diagnosis and refer patients to mental health professionals only to help them cope with the stresses involved with MCS.

The greatest conflict between allergists and clinical ecologists revolves around the method known as provocation-neutralization, which clinical ecologists and otolaryngological (ear, nose, and throat) allergists use for both diagnosis and treatment. A small dose of a chemical or food is injected under the skin or placed under the tongue to provoke a response and the patient is then observed for symptoms and/or an increase in wheal size if the agent is injected. Next, various dilutions of the substance that produced symptoms are injected or given sublingually until a dilution is found that turns off the patient's symptoms or causes no expansion in wheal size after an intradermal injection. This dose is called the neutralizing dose.

Otolaryngological allergists and clinical ecologists have conducted controlled studies of the efficacy of provocation-neutralization and concluded from these that the method is effective. In contrast, traditional allergists and others have conducted similar controlled studies and concluded that provocation-neutralization is not effective.

The articles and position statements written about these negative studies imply that since provocation-neutralization seems to be ineffective, the symptoms of MCS must not be caused by reactions to chemicals or foods, and so MCS is not an illness caused by chemicals or foods. Such arguments confuse the efficacy of a method of diagnosing and treating an illness with the existence of the illness, Ashford says. It is as if researchers were to test the efficacy of a particular cancer therapy—the use of laetrile, for example—and from this research, conclude information about the existence of cancer.

A number of medical scientists have raised serious questions about the validity of the controlled studies of

People with MCS can be divided into four categories

Group	Nature of exposure	Demographics
Industrial workers	Acute and chronic exposure to industrial chemicals	Primarily male; blue collar; 20 to 65 years old
Tight-building occupants	Off-gassing from construction materials; office equipment or supplies; tobacco smoke; inadequate ventilation	Female more than male; white-collar office workers and professionals; 20 to 65 years old; schoolchildren
Contaminated communities	Toxic waste sites; aerial pesticide spraying; groundwater contamination; air contamination by nearby industry and other community exposures	Male and female, all ages; children or infants may be affected first or most; fetuses could possibly be affected; middle to lower class
Individuals	Heterogeneous—indoor air (domestic); consumer products; drugs; and pesticides	70–80% female; 50% 30 to 50 years old; white, middle to upper class and professionals

Source: "Chemical Exposures: Low Levels and High Stakes," by Nicholas A. Ashford and Claudia S. Miller, Van Nostrand Reinhold, New York, N.Y., 1991, page 4

provocation-neutralization. Because of poor design, all studies done to test the efficacy of provocation-neutralization are flawed, says Miller.

Two medical societies, the American College of Physicians and the American Academy of Allergy & Immunology, have written position statements on clinical ecology that are based largely on evidence for the ineffectiveness of provocation-neutralization therapy. The American College of Physicians devoted about half its statement to a discussion of such therapy and concluded that it is unproven. Most frequently, MCS patients have symptoms of somatic or psychologic dysfunction or both, the ACP statement asserts. Proof of cause-effect relations between environmental factors and symptoms of MCS is difficult, the statement says, because such a broad range of agents are implicated. "The existence of [MCS] as presented in clinical ecology theory must be questioned because of a lack of a clinical definition," the statement continues.

In its most recent position statement, the American Academy of Allergy & Immunology devotes considerable space to a discussion of the lack of evidence for abnormalities in the immune systems of MCS patients and refers to a previous position statement that finds provocation-elimination technique ineffective. Like the American College of Physicians, it concludes from this discussion that there is no clear evidence that many of the symptoms of MCS patients are related to allergy, sensitivity, toxicity, or any other type of reaction from foods, water, chemicals, pollutants, viruses, and bacteria. "Anecdotal articles do not constitute sufficient evidence of a cause-and-effect relationship between symptoms and environmental exposure," it says. The American Medical Association is preparing a position statement on clinical ecology that will be released later this year.

Environmental control unit

Many physicians would like to use an environmental control unit for diagnosis of difficult MCS cases, but currently no such units are operating in the U.S. First developed in 1975 and operated in a Chicago hospital by the founder of clinical ecology, Theron G. Randolph, who practices in the Chicago area, an environmental control unit is a specially constructed set of rooms, usually one wing of a hospital, made of materials like ceramic tile that do not release volatile organic compounds and with furnishings made of natural materials. The rooms have air filters to remove contaminants. Chemically sensitive patients can live in these units for weeks at a time, fast for four to seven days, and gradually be exposed to chemicals and foods, one at a time, to see which ones provoke their symptoms. This diagnostic method is time-consuming and extremely expensive, but it provides answers that are difficult to learn in any other way. Clinical ecologist Rea and allergist Selner each used to have an environmental control unit, but both units have been closed for reasons unrelated to their possible utility as a research tool. At this time, the only operating environmental units are located in Germany, England, and China.

There are two reasons for using environmental control units. Some physicians believe patients become adapted to chemicals in their everyday environment and must be de-adapted for several days before their true reactions to these can be tested. For example, when people from the northern plains of Canada are placed in a chamber and exposed to ozone, they react to it much more strongly than similar subjects from Los Angeles, who have already adapted to daily doses of ozone. Researchers theorize that the same adaptive mechanism operates with other chemicals.

Also, "people are often exposed to dozens of different incitants simultaneously and literally hundreds of different incitants over the course of a single day, so that any health effects of these may overlap, making it difficult to discern cause-and-effect relationships," says Miller. Use of an environmental control unit can overcome the problems of overlapping exposures, Miller explains.

Research priorities

No matter what their beliefs are about the probable cause of MCS, researchers agree that double-blind, placebo-controlled studies should be conducted in an environmental control unit to see whether MCS patients do indeed react to low-level chemical exposures. At the workshop on MCS arranged by NAS, the participants decided that such studies are a major research priority.

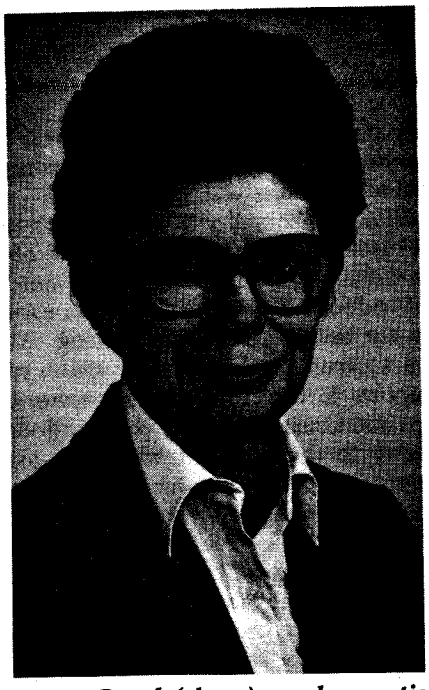
Physicians have widely different expectations about the results of this research, however. Researchers who think exposure to chemicals is the cause of MCS expect these studies will bear them out.

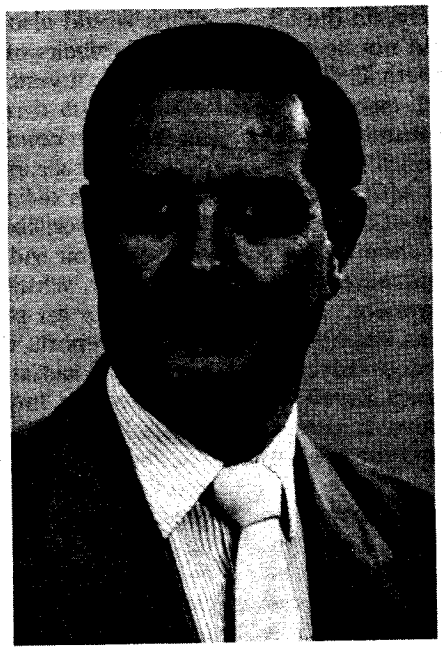
On the other hand, if the mechanism of MCS is entirely psychological, studies using an environmental unit may show that chemicals do not cause these patients' problems. Such a negative result would be hard to prove any other way. Thus DeHart, who calls an environmental control unit a "red herring," still advocates its use. "I think it has to be done," he says, "because it's the only unique thing that the clinical ecologists have [developed]."

At the NAS workshop, the participants also agreed on the outlines of a number of other research projects. A uniform database should be collected that includes detailed information about patients' sensitivity to foods, chemicals, and drugs; their dietary, smoking, and medication histories; and psychological screening information.

The participants urged that a double-blind, placebo-controlled procedure be used in testing the effects on patients of individual chemicals and recommended that responses of patients and control subjects to exposures be probed with immunologic, neurologic, endocrinologic, psychological, and social markers and measures. The experts also recommended that animal models that mimic the human syndrome be developed.

Several different types of epidemiological studies were recommended. First, a case-comparison study involving occupational/environmental medical clinics across the U.S. would enroll patients who say they respond to low levels of chemicals. Psychologic-psychiatric conditions, immune function, and neurotoxic reactions would be measured in these patients and suitable





Gresch (above): psychosomatic symptoms. DeHart: fears new disease by fiat

controls. The information from the multiclinic study would then be used to study the prevalence of MCS in the general population.

Populations affected by events involving a toxic exposure—for example, those living near a large chemical spill or working in a contaminated workplace—should also be characterized and followed as the disease progresses. Ashford and Miller describe this as dynamic toxicology.

Currently, the federal government is not funding any research that is specifically designed to study MCS, though it does fund related research that could help in understanding the syndrome. For example, the Consumer Product Safety Commission conducted telephone interviews of people who claim injury from exposure to new carpeting. Some of these appear to be MCS patients. Robert Axelrad, head of the indoor air division at EPA, says that after the NAS workshop proceedings on chemical sensitivity are published this fall, EPA may use them to try obtain funding for research on the syndrome.

Even though current government regulations provide some very limited benefits and protections to MCS patients, some patients become so severely disabled that they can't take advantage of these benefits. Severely affected MCS patients may have difficulty leaving their homes because of the multitude of chemical exposures they encounter in public buildings or from automobiles. Even worse, they may lose their jobs because they can't tolerate exposures encountered in the workplace. Without work, many become poor, anxious, and depressed. "There is no secondary gain for these patients. They are becoming very poor, very fast," Cullen says.

Possible solutions

Research to determine precise mechanisms and effective treatment for MCS may require many years. For example, it has taken 50 years to begin to understand the subtle effects lead has on the human body. Research on the effects of multiple chemicals, if any, could take even longer. In the meantime, what can be done?

Not even the most outspoken patient advocates recommend cutting back chemical exposures for everyone so drastically that none of the current MCS patients are affected by exposures to such common substances as automobile emissions. Such a change would probably be technologically infeasible, economically disasterous, and would require revolutionary changes by all of society.

Patient advocates, however, do recommend some fairly simple changes they believe would make life easier for patients, help prevent further cases, and help protect everyone's health. Mary Lamielle, founder and president of the patient advocacy group, the National Center for Environmental Health Strategies (NCEHS), calls for making the current ventilation recommendations of the American Society of Heating, Refrigeration & Air-Conditioning Engineers (ASHRAE) a minimum national mandatory standard for all public and commercial buildings. She would also prohibit smoking in all public buildings.

Lamielle's center would also prohibit a number of products now used quite widely in public buildings: deodorizers that cause toxic or allergenic reactions in some people, olfactory nerve anesthetics, scents or perfumes that are used to affect the behavior or mood of occupants, and products other than pesticides containing *p*-dichlorobenzene. "Many people with chemical sensitivity experience debilitating symptoms from deodorizing agents being pumped through building ventilation systems or spritzed into rooms," Lamielle says. To avoid spraying of insecticides in public buildings, NCEHS calls for other pest control methods when feasible.

The center also would like EPA to develop product labeling for consumer products like new carpets that emit volatile organic compounds. Labels should provide meaningful information on individual ingredients as well as the total content of volatile organic compounds. In addition, listing of toxic, sensitizing, or allergenic substances on the labels for all consumer products would be mandatory.

Moreoever, NCEHS wants Congress to appropriate funds for research and education on MCS and for emergency assistance to MCS victims who are homeless or threatened with loss of their homes. It requests that EPA prepare a report to Congress on chemical sensitivity, including MCS, and that a nationwide registry of chemical sensitivity complaints be developed.

"What we are really after is not lawsuits, but protection of people's basic human rights to a healthy environment and some medical assistance," says Davis, adviser to NCEHS.

Representatives of the chemical industry, on the other hand, think regulatory changes should not be made until more is learned about MCS. Elizabeth E. Gresch, physician and senior occupational health associate for Dow Chemical, is one of a very small number of experts on this issue employed by the chemical industry. Gresch considers the symptoms of many MCS patients psychosomatic. She doesn't think that any of those who are diagnosed with MCS are reacting to chemicals, except for the individuals with well-recognized allergies to a specific chemical like toluene diisocyanate.

The Chemical Manufacturers Association has not taken an official position on MCS. But it does advocate well-conducted research in this area, says Karen W. Creedon, CMA's manager for health issues. It also intends to adopt the views of the traditional medical establishment on MCS.

The organization has prepared a briefing paper on MCS, which it calls environmental illness. In this paper, CMA cites some of the arguments of experts who believe MCS is caused by psychological factors and omits the arguments of those who think MCS is caused by chemicals. "Nationally known experts in the fields of allergy, immunology, and internal medicine say the assertion that environmental illness [MCS] is a legitimate disease is unproven," the paper states. "Emphasis should be placed on proper psychological diagnosis and treatment rather than upon false labels and therapy that can ultimately prolong their [MCS patients'] impairment," it continues. But CMA encourages sympathy for the patients, saying "these patients are ill and deserving of compassion, understanding, and expert medical care." At the end of the briefing paper, CMA encourages the formation of a coalition of manufacturers of pesticides, soaps and detergents, along with medical associations, insurance companies, the aerospace industry, automobile manufacturers, and others who have "an interest in placing environmental illness [MCS] in its proper perspective."

The Business Council on Indoor Air, an association of engineering firms for ventilation systems, commercial building owners and tenants, and manufacturers of chemicals and building materials, recommends that the current ventilation recommendations for public buildings should be made mandatory. Proper design of ventilation systems in buildings might prevent a lot of future health problems—outbreaks of sick-building syndrome as well as perhaps MCS, says Stewart E. Holm, director of scientific affairs for the council. However, at this time the council does not advocate regulatory changes that are specifically designed to alleviate or prevent MCS. "Because of the controversy surrounding environmental illness [MCS], it is premature to develop any governmental policy based on the vague and anecdotal information currently available," the council says in a position paper on MCS.

The separate indoor air bills introduced this year in the House and Senate both contain provisions that could help people who are chemically sensitive and possibly prevent future cases, if, indeed, MCS is triggered by excessive exposure to chemicals. These provisions would also help prevent sick-building syndrome and outbreaks of classic allergies to individual chemicals and conventional allergens.

Both bills direct EPA, in coordination with other agencies, to conduct research on the human health effects of indoor air contaminants. And they both would establish an office of indoor air quality at EPA to centralize responsibility for assessing and improving the quality of air indoors. Currently, EPA has a division of indoor air, which reports to the office of atmospheric and indoor air programs. Creating an office of indoor air that reports directly to the assistant administrator for air and radiation would give indoor air issues more visibility and importance on the agency's agenda.

The House bill, however, has several provisions that are more regulatory than the Senate bill. It directs EPA and CPSC to develop appropriate labels for all building products posing significant adverse health effects and to educate consumers about the meanings of these labels. Also, it establishes mandatory minimum ventilation standards, those recommended by ASHRAE, for all public and commercial buildings. In contrast, the Senate bill requires EPA only to analyze the adequacy of existing ventilation standards.

Gresch says representatives of the chemical industry expect indoor air legislation to pass this year. However, Holm does not think Congress will have enough time to work on indoor air bills in 1991 because it will be too busy with other environmental legislation, such as the Clean Water Act and the Resource, Conservation & Recovery Act. No matter what happens with the indoor air bills this year, observers expect that some government funding, from existing programs if not from new indoor air legislation, will soon be forthcoming to do research on MCS, particularly for constructing and operating an environmental control unit.

To use Winston Churchill's phrase for describing Russia, MCS is "a riddle, wrapped in a mystery inside an enigma." Medical scientists do not agree on whether MCS is a unique syndrome. Some progress is being made on developing one or more operational definitions of MCS for particular purposes. Measures of intensity of affliction for individual patients are subjective. Research tools are primitive. No unified theory of the disease has emerged. Bureaucrats have equivocated, and Congress discusses.

Meanwhile, notices for about 50 new chemical compounds are submitted to EPA for introduction into commerce each week, and some unidentifiable and likely growing number of individuals live distorted lives allegedly because of their exposure to chemicals. At the same time, most of us go on enjoying the benefits of chemistry. □

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